

We claim:

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1. A chimeric protein for detecting the presence or activity of a pre-determined protease, which comprises:
 - 5 a) a repressor domain which represses activity of a normally biologically active protein fused thereto;
 - b) a reporter domain comprising a protein having a detectable biological activity when not fused to the repressor domain; and
 - c) a protease cleavage domain linking the repressor domain to
10 the reporter domain, the protease cleavage domain comprising a structure that is cleaved by activity of the pre-determined protease.
 - 15 2. The chimeric protein of claim 1, wherein the repressor domain comprises a hormone binding domain of a steroid hormone receptor.
 3. The chimeric protein of claim 1, wherein the reporter domain comprises β -glucuronidase.
 - 20 4. The chimeric protein of claim 1, wherein the protease cleavage domain comprises a cleavage site for a caspase.
 5. The chimeric protein of claim 1, which further comprises a spacer
25 between the protease cleavage domain and one or both of the repressor domain and the reporter domain.
 6. The chimeric protein of claim 1, which comprises at least one repressor domain and a plurality of reporter domains, each linked to the at least one repressor domain by a protease cleavage site.
 - 30 7. The chimeric protein of claim 7, wherein the plurality of reporter domains are different from one another.

8. The chimeric protein of claim 7, wherein the protease cleavage sites
are different from one another.

9. A chimeric protein for measuring caspase activity, comprising a
5 hormone binding domain linked to a β -glucuronidase enzyme by a peptide comprising
a caspase cleavage site, wherein the β -glucuronidase is inactive due to linkage to the
hormone binding domain and release of the β -glucuronidase through caspase cleavage
of the cleavage site restores activity of the β -glucuronidase.

10. A method for determining the presence or activity of a pre-
determined protease in a biological sample, which comprises:

a) providing a chimeric protease detector protein comprising:

i) a repressor domain which represses activity of a
normally biologically active protein fused thereto;

15 ii) a reporter domain comprising a protein having a
detectable biological activity when not fused to the repressor domain; and

iii) a protease cleavage domain linking the repressor
domain to the reporter domain, the protease cleavage domain comprising a structure
that is cleaved by activity of the pre-determined protease;

20 b) adding the protease detector protein to the biological sample
suspected of containing the pre-determined protease; and

c) measuring the detectable biological activity, if any, of the
reporter domain, the occurrence and amount of the detectable biological activity being
proportional to the occurrence and amount of the pre-determined protease in the
25 biological sample.

11. The method of claim 10, wherein the biological sample comprises
a biological fluid, tissue or cell extract and the protease detector protein is provided as
an isolated protein.

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12. The method of claim 10, wherein the biological sample comprises

intact cells in which the pre-determined protease, if present, is contained, and the protease detector protein is provided by introducing into the cells an expressible DNA construct that encodes the protein, under conditions whereby the protein is expressed.

5 13. The method of claim 12, wherein the expressible DNA construct is introduced into the cells by transient transformation.

14. The method of claim 12, wherein the expressible DNA construct is introduced into the cells by stable transformation.

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15. The method of claim 10, adapted for determining the presence or amount of a plurality of pre-determined proteases.

15 16. The method of claim 15, wherein the plurality of proteases are detected by adding a plurality of protease detector proteins, each having a protease cleavage domain specifically cleaved by one of the pre-determined proteases, and each having a differentially detectable reporter domain.

20 17. The method of claim 15, wherein the plurality of proteases are detected by adding one or more modified protease detector proteins, each comprising a repressor domain linked to two different protease cleavage domain, each protease cleavage domain being linked to a differentially detectable reporter domain.

25 18. A method for determining if a test compound affects the amount or activity of a pre-determined protease, the method comprising:

a) providing a chimeric protease detector protein comprising:

i) a repressor domain which represses activity of a normally biologically active protein fused thereto;

30 ii) a reporter domain comprising a protein having a detectable biological activity when not fused to the repressor domain; and

iii) a protease cleavage domain linking the repressor

domain to the reporter domain, the protease cleavage domain comprising a structure
that is cleaved by activity of the pre-determined protease;

b) preparing a test sample and a control sample, the test sample
containing the pre-determined protease, the protease detector protein and the test
5 compound, the control sample containing the pre-determined protease and the
protease detector protein;

c) measuring the detectable biological activity, if any, of the
reporter domain, in the test sample and the control sample; and

d) comparing the amount of the detectable biological activity in
10 the test sample with that in the control sample, an increase or decrease of the activity
in the test sample being indicative of the ability of the test compound to affect the
amount or activity of the protease.

19. A test kit for detecting the presence or activity of a pre-determined
15 protease, which comprises a container containing:

a) a chimeric protease detector protein comprising:

i) a repressor domain which represses activity of a
normally biologically active protein fused thereto;

ii) a reporter domain comprising a protein having a
20 detectable biological activity when not fused to the repressor domain; and

iii) a protease cleavage domain linking the repressor
domain to the reporter domain, the protease cleavage domain comprising a structure
that is cleaved by activity of the pre-determined protease;

b) optionally, at least one other reagent for using the protease
25 detector protein; and

c) optionally, instructions for using the protease detector
protein.

20. The test kit of claim 19, adapted for detection of a plurality of pre-
30 determined proteases, which comprises a plurality of chimeric protease detector
proteins.